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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/458,014	12/10/1999	JACQUES DUMAS	BAYER11-C1	8328

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EXAMINER	
CHONG, YONG SOO	
ART UNIT	**PAPER NUMBER**
1617	

MAIL DATE	DELIVERY MODE
07/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/458,014	DUMAS ET AL.	
	Examiner	Art Unit	
	Yong S. Chong	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *6/11/07*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-34,37-55 and 57* is/are pending in the application.

4a) Of the above claim(s) *5-27,37,39-41,52 and 53* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4, 28-34, 38, 42-51, 54-55, 57* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 5/4/2005 has been entered.

This Office Action is in response to applicant's response filed on 6/11/2007. Applicant's election **with** traverse of the restriction requirement in the reply is acknowledged. The traversal is on the ground(s) that all of the groups are classified in the same group class and subclass. This is not found persuasive because the groups are classified under different class and subclass with only the elected Group V under class 514 and subclass 385. Therefore, since the groups are classified in different class and subclass, a search for one will not lead to information regarding another because there is no common core structure. The requirement is still deemed proper and is therefore made FINAL.

Claim(s) 35-36, 56 have been cancelled. Claim(s) 1-34, 37-55, 57 are pending. Claim(s) 1, 42, 50, 52, 55 have been amended. Claim(s) 5-27, 39-41, 52-53 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Claim(s) 37 is withdrawn from further consideration as being drawn to a non-elected species. Claim(s)

1-4 (in part), 28-34 (in part), 38, 42-51 (in part), 54-55 (in part), 57 (in part) are examined herein insofar as they read on the elected invention and species.

Applicant's amendments have rendered all rejections of the last Office Action moot, therefore hereby withdrawn. The following new rejections will now apply.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4 (in part), 28-34 (in part), 38, 42-51 (in part), 54-55 (in part), 57 (in part) are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement for a method for the treatment of a disease mediated by p38 other than cancer comprising administering a compound of formula I. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The instant specification fails to provide information that would allow the skilled artisan to fully practice the instant invention without undue experimentation. Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547, the court recited eight factors: (1) the nature of the invention; (2) the state of the prior

art; (3) the breadth of the claims; (4) the amount of direction or guidance presented; (5) the predictability or unpredictability of the art; (6) the relative skill of those in the art; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary.

(1) The Nature of the Invention: The rejected claims are drawn to an invention which pertains to a method for the treatment of a disease mediated by p38 other than cancer comprising administering a compound of formula I.

(2) State of the Prior Art: The state of the art regarding p38 inhibition has shown to inhibit both cytokine production (TNFα, IL-1, IL-6, IL-8) and proteolytic enzyme production (MMP-1, MMP-3). Clinical studies have linked TNFα production to a number of inflammatory and/or immunomodulatory diseases. There is no indication that such a link actually translates to treatment of the disease. Thereofore, the same argument can be applied to p38 inhibition.

(3) Breadth of Claims: The complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. The claims encompass virtually every disease or disorder that is mediated by p38 kinase. Furthermore, p38 kinase is disclosed to inhibit both cytokine production (TNFα, IL-1, IL-6, IL-8) and proteolytic enzyme production (MMP-1, MMP-3). Therefore, the invention is complex because it involves any disease or disorder related to these cytokines or enzymes as being within the scope of this invention.

(4) Guidance of the Specification: The guidance of the specification discloses a pathway between inhibition of p38 and various inflammatory and/or immunomodulatory

diseases through cytokine production (TNFα, IL-1, IL-6, IL-8) and proteolytic enzyme production (MMP-1, MMP-3). The specification does not disclose how to determine whether a disease or disorder can be treated by p38 inhibition, it only discloses that the two are linked together. As a result, one of ordinary skill in the art would be forced to perform an exhaustive search for the embodiments of any drug having the function recited in the instant claims suitable to practice the invention. Furthermore, one of ordinary skill in the art would have to determine not only which compounds inhibit p38, but which compounds are therapeutically effective on a p38 mediated disease. The specification shows examples of *in vitro* p38 inhibition but does not provide any raw data or what specific compounds were tested. The *in vivo* study was not performed on subjects with any diseases or disorders.

(5) The Predictability or Unpredictability of the Art: The invention is directed to a method for the treatment of a disease mediated by p38 other than cancer comprising administering a compound of formula I. Treatment of a disease involves many biochemical pathways mediated by many different proteins. It is not possible to predict the efficacy in the treatment of a disease simply by inhibition of p38.

Moreover, one of skill in the art would recognize that it is highly unpredictable in regard to therapeutical effects, side effects, and especially serious toxicity that may be generated by drug-drug inerteractions when and/or after adminstering to a host (e.g., a human) any compound represented by formula I. See "Goodman & Gilman's The Pharmacological Basis of Therapeutics" regarding possible drug-drug interactions (9th ed., 1996), page 51 in particular. *Goodman & Gilman* teaches that "The frequency of

significant beneficial or adverse drug interactions is unknown" (see the bottom of the left column of page 51) and that "Recognition of beneficial effects and recognition of and prevention of adverse drug interactions require a thorough knowledge of the intended and possible effects of drugs that are prescribed" and that "The most important adverse drug-drug interactions occur with drugs that have serious toxicity and a low therapeutic index, such that relatively small changes in drug level can have significant adverse consequences" (see the right of page 51) (emphasis added). In the instant case, in the absence of fully recognizing the identity of the member genus herein, one of skill in the art would not be able to fully predict possible adverse drug-drug interactions occurring with many combinations of any compounds having the claimed functional properties in the pharaceutical compositions herein. Thus, the teachings of *Goodman & Gilman* clearly support that the instant claimed invention is highly unpredictable.

(6) The Relative Skill of those in the Art: One of ordinary skill in the art knows how to inhibit p38 and how to effectively treat various inflammatory and/or immunomodulatory diseases, but does not know how to treat diseases that are not inflammatory or immunomodulatory by nature by inhibiting p38.

(7) Working Examples: The specification lacks any working examples of treating a p38 mediated disease comprising administering a compound of formula I. The only examples are drawn to an *in vitro* p38 kinase inhibition assay and *in vivo* inhibition of TNFα in mice. Examiner notes that there is no raw data for any of the disclosed compounds for either of these examples. Moreover, the mice are not disclosed to have

a p38 mediated disease or disorder, therefore no disease is being treated in the examples.

(8) The Quantity of Experimentation Necessary: The specification fails to provide support for a method for the treatment of a disease mediated by p38 other than cancer comprising administering a compound of formula I. A large quantity of experimentation would be needed in order to discover what diseases or disorders can be treated by inhibition of p38 and to what extent. Nor does it provide information to practice the claimed invention, absent undue experimentation. Genetech, 108 F. 3d at 1366 states that "a patent is not a hunting license. It is not a reward for search, but compensation for its successful conclusion" and "patent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable."

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yong S. Chong whose telephone number is (571)-272-8513. The examiner can normally be reached on M-F, 9-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, SREENI PADMANABHAN can be reached on (571)-272-0629. The fax phone number for the organization where this application or proceeding is assigned is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

YSC

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER

7/20/07